

That which is claimed is:

1. An isolated polypeptide comprising a Death Domain (DD), Death Effector Domain (DED), or NB-ARC domain,  
5 said domain comprising an amino acid sequence at least 60% identical to the amino acid sequence set forth in any of SEQ ID NOS:2, 4, 6, 8, 10, 12, 53, 56 or 58, provided said polypeptide does not consist of the sequence of any of SEQ ID NOS:14, 24, 28, 55 or 57.
- 10 2. An isolated polypeptide comprising a DD, DED, or NB-ARC domain, said domain comprising the amino acid sequence set forth in any of SEQ ID NOS:2, 4, 6, 8, 10, 12, 53, 56 or 58, provided said polypeptide does not consist of the sequence of any of SEQ ID NOS:14, 24, 28, 55 or 57.
- 15 3. An isolated polypeptide comprising an amino acid sequence at least 60% identical to the amino acid sequence set forth in any of SEQ ID NOS: 16, 18, 20, 22, or 26, provided said polypeptide does not consist of the sequences of any of SEQ ID NOS: 24 and 28.
- 20 4. An isolated polypeptide comprising an amino acid sequence set forth in any of SEQ ID NOS: 16, 18, 20, 22, or 26.
- 25 5. An isolated polypeptide consisting of a DD, DED, or NB-ARC domain of any of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 53, 56 or 58.

6. An isolated anti-DD, anti-DED, or anti-NB-ARC domain antibody having specific reactivity with a polypeptide according to claim 5.

7. An isolated antibody having specific  
5 reactivity with a polypeptide of SEQ ID NO: 18 or 22.

8. The antibody according to claim 6 or 7, wherein said antibody is a monoclonal antibody.

9. A cell line producing a monoclonal antibody of claim 8.

10 10. The antibody according to claim 6 or 7, wherein said antibody is a polyclonal antibody.

11. A chimeric protein comprising a DD, DED, or NB-ARC domain of claim 1 or 2.

12. An isolated peptide, comprising at least 10  
15 contiguous amino acids of any of SEQ ID NOS: 18 and 22.

13. An isolated peptide, comprising between 10 and 100 contiguous amino acids of a DD, DED, or NB-ARC domain of claim 5.

14. An isolated nucleic acid molecule encoding a DD, DED, or NB-ARC domain-containing polypeptide selected from:

5 (a) DNA encoding the amino acid sequence set forth in any of SEQ ID NOS:2, 4, 6, 8, 10, 12, 53, 56 or 58; or

10 (b) DNA that hybridizes to the DNA of (a) under moderately stringent conditions, wherein said DNA encodes a biologically active DD, DED, or NB-ARC domain,

provided said nucleic acid molecule does not consist of a nucleic acid molecule encoding the amino acid sequence of any of SEQ ID NOS:14, 24, 28, 55 or 57.

15 15. A vector containing a nucleic acid molecule of claim 14.

16. Recombinant cells containing a nucleic acid molecule of claim 14.

17. An isolated nucleic acid molecule encoding a polypeptide selected from:

(a) DNA encoding the amino acid sequence set forth in any of SEQ ID NOS:16, 18, 20, 22, or 26;  
5 or

(b) DNA that hybridizes to the DNA of (a) under moderately stringent conditions, wherein said DNA encodes a biologically active DD, DED, or NB-ARC domain,

10 provided said nucleic acid molecule does not consist of a nucleic acid molecule encoding the amino acid sequence of any of SEQ ID NOS:24, and 28.

18. An isolated nucleic acid molecule encoding a DD, DED, or NB-ARC domain set forth in any of SEQ ID NOS:1,  
15 3, 5, 7, 9, 11, or 52 provided said nucleic acid molecule does not consist of a nucleic acid molecule encoding the sequence of any of SEQ ID NOS:13, 23, 27, or 54.

19. An isolated nucleic acid molecule encoding a polypeptide set forth in any of SEQ ID NOS: 15, 17, 19, 21,  
20 or 25 provided said nucleic acid molecule does not consist of a nucleic acid molecule encoding the amino acid sequence of any of SEQ ID NOS:23, and 27.

20. An oligonucleotide comprising between 15 and 300 contiguous nucleotides with a sequence set forth in any  
25 of SEQ ID NOS:1, 3, 5, 7, 9, 11, 17, 21 or 52.

21. Single strand DNA primers for amplification of DD, DED or NB-ARC domain nucleic acid, wherein said primers comprise a nucleic acid sequence derived from the nucleic acid sequences set forth as SEQ ID NOS:1, 3, 5, 7,  
5 9, 11 or 52.

22. A kit for detecting the presence of a DD, DED or NB-ARC domain cDNA sequence comprising at least one oligonucleotide according to claim 20.

23. A method for expression of a DD, DED or  
10 NB-ARC domain, said method comprising culturing cells of claim 16 under conditions suitable for expression of said DD, DED or NB-ARC domain.

24. A method for detecting a nucleic acid molecule encoding a DD, DED or NB-ARC domain, said method  
15 comprising contacting a sample containing nucleic acid molecules with an oligonucleotide according to claim 20, wherein said contacting is effected under high stringency hybridization conditions, and identifying nucleic acid molecules which hybridize thereto.

20 25. A method for detecting the presence of a DD, DED, or NB-ARC domain in a sample, said method comprising contacting a test sample with an antibody according to claim 6, detecting the presence of an antibody:DD, DED, or NB-ARC domain complex, and therefor detecting the presence of a DD,  
25 DED or NB-ARC domain in said test sample.

26. A method of identifying a binding agent that binds a DD, DED or NB-ARC domain, comprising the steps of:

- 5           a)    contacting a DD, DED, or NB-ARC domain from DAP3, IRAK4, CTDD, DED4 or NIDD with a candidate binding agent; and
- b)    detecting the association of said domain and said candidate binding agent,

          wherein said association identifies said candidate binding agent as a binding agent that binds a DD, DED, or NB-ARC  
10   domain from DAP3, IRAK4, CTDD, DED4 or NIDD.

27. The method of claim 26, wherein said association is detected by a method selected from the group consisting of yeast two hybrid assay, immunoprecipitation, SPA, UV or chemical crosslinking, NMR, MS, and FPA.

15           28. The method of claim 26, where said binding agent is a protein.

29. The method of claim 26, where said binding agent is a drug.

30. A method of identifying an effective agent that modulates the association of a DD, DED or NB-ARC domain with a protein that binds said DD, DED or NB-ARC domain, comprising the steps of:

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a) contacting said proteins under conditions that allow said DD, DED, or NB-ARC domain and said protein that binds said DD, DED or NB-ARC domain to associate with an agent suspected of being able to modulate the association of said DD, DED or NB-ARC domain protein and protein that binds said DD, DED or NB-ARC domain; and

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b) detecting the modulated association of said DD, DED or NB-ARC domain and said protein that binds said DD, DED, or NB-ARC domain, wherein said modulated association identifies an effective agent,

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wherein said DD, DED, or NB-ARC domain is from DAP3, IRAK4, CTDD, DED4 or NIDD.

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31. The method of claim 30, wherein said association is detected by a method selected from the group consisting of yeast two hybrid assay, immunoprecipitation, SPA, UV or chemical crosslinking, NMR, MS, and FPA.

32. The method of claim 30, wherein said altered association is detected by measuring the activity of NF- $\kappa$ B.

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33. The method of claim 30, wherein said altered association is detected by measuring the activity of caspase-8.

34. The method of claim 30, wherein said  
5 effective agent is a drug.

35. The method of claim 30, wherein said effective agent is a protein.

36. A method of modulating a cell process comprising contacting a cell with an effective amount of an  
10 agent identified by the method of claim 30 that modulates the activity of a DD-, DED-, or NB-ARC domain, wherein said cell process is selected from the group consisting of apoptosis, cell proliferation, cell adhesion, cell stress responses, responses to microbial infection, and B cell  
15 immunoglobulin class switching.

37. The method of claim 36, where the cell process is apoptosis.

38. A method for modulating an activity mediated by a DD, DED or NB-ARC domain, said method comprising  
20 contacting said DD, DED or NB-ARC domain with an effective amount of an agent identified by claim 30.



39. The method of claim 38, wherein said modulated activity is selected from the group consisting of: binding of a DD, DED or NB-ARC domain protein to a protein that binds a DD, DED or NB-ARC domain, NF- $\kappa$ B activity,  
5 caspase activity, apoptosis activity, cell proliferation activity, cell adhesion, cell stress response activity, responses to microbial infection activity, and B cell immunoglobulin class switching activity.

40. The method of claim 39, where the modulated  
10 activity is apoptosis activity.

41. A method of modulating the activity of NF- $\kappa$ B comprising contacting a cell with an effective amount of an agent identified by claim 30 that modulates the activity of a DD-containing or NB-ARC-domain.

15 42. A method of modulating the activity of a caspase comprising contacting a cell with an effective amount of an agent identified by claim 30 that modulates the activity of a DD-, DED-, or NB-ARC domain.

43. A method of modulating the level of a cell  
20 process within a cell, comprising the steps of:

a) introducing a nucleic acid molecule encoding a DD, DED or NB-ARC domain into the cell; and

b) expressing said DD, DED or NB-ARC domain in said cell, wherein the expression of said DD, DED or NB-ARC domain modulates a cell process within  
25 said cell,

wherein said DD, DED, or NB-ARC domain is from DAP3, IRAK4, CTDD, DED4 or NIDD, and wherein said cell process is selected from the group consisting of apoptosis, cell proliferation, cell adhesion, cell stress responses, responses to microbial infection, and B cell immunoglobulin class switching.

44. The method of claim 43, where the cell process is apoptosis.

45. A method of modulating a cell process within a cell, comprising introducing into a cell an antisense nucleotide sequence that specifically hybridizes to a nucleic acid molecule encoding a DD, DED or NB-ARC domain from DAP3, IRAK4, CTDD, DED4 or NIDD, wherein said hybridization reduces or inhibits the expression of said DD, DED or NB-ARC domain in said cell, and wherein said cell process is selected from the group consisting of apoptosis, cell proliferation, cell adhesion, cell stress responses, responses to microbial infection, and B cell immunoglobulin class switching.

46. The method of claim 45, where the cell process is apoptosis.

47. A method of modulating a cell process comprising contacting a cell with a compound selected from the group consisting of: a DD, DED or NB-ARC domain or functional fragment thereof, an agent identified according to claim 30, and an anti-DD, anti-DED or anti-NB-ARC domain antibody wherein said DD, DED, or NB-ARC domain is from DAP3, IRAK4, DED4 or NIDD.

48. A method of diagnosing a pathology characterized by an increased or decreased level of a DD, DED or NB-ARC domain in a subject, comprising the steps of:

5 a) contacting a test sample from said subject with an agent that can bind said DD, DED or NB-ARC domain under suitable conditions, which allow specific binding of said agent to said DD, DED or NB-ARC domain; and

10 b) comparing the amount of said specific binding in said test sample with the amount of specific binding in a control sample, wherein an increased or decreased amount of said specific binding in said test sample as compared to said control sample is diagnostic of a pathology,

15 and wherein said DD, DED, or NB-ARC domain is from DAP3, IRAK4, CTDD, DED4 or NIDD.

49. The method of claim 48, wherein said agent is an anti-DD, anti-DED, or anti-NB-ARC domain antibody, FADD, caspase-8, caspase-10, DR4, DR5, Traf6, hToll, MyD88 Fas, 20 Raidd, IRAK, IRAK-2, IRAK-M, p75NTR, Tradd, DAP kinase, RIP, NMP84, ankyrins, Flip, PEA15, Flash, BAP31, BAR, DEDT/DEDD, CTDD, or DAP3.

50. A method of diagnosing a pathology characterized by an increased or decreased level of a DD, DED or NB-ARC domain in a subject, comprising the steps of:

- 5 a) contacting a test sample containing nucleic acid molecules from said subject with an oligonucleotide according to claim 20 wherein said contacting is effected under high stringency hybridization conditions, and
- 10 b) comparing the amount of specific binding in said test sample with the amount of specific binding in a control sample, wherein an increased or decreased amount of said specific binding in said test sample as compared to said control sample is diagnostic of a pathology,
- 15 and wherein said DD, DED, or NB-ARC domain is from DAP3, IRAK4, CTDD, DED4 or NIDD.

51. A method of detecting a *Chlamydia* infection, comprising contacting a test sample from a subject with an antibody specifically reactive with a peptide or polypeptide

20 consisting of any of SEQ ID NOS:10, 20, 53, 56 or 58, wherein binding of said sample to said antibody indicates that said subject has a *Chlamydia* infection.

52. A method of detecting a *Chlamydia* infection, comprising contacting a nucleic acid containing test sample from a subject with a nucleic acid molecule encoding any of SEQ ID NOS:10, 20, 53, 56, or 58, wherein said contacting is  
5 effected under high stringency hybridization conditions, and wherein binding of said sample with said nucleic acid molecule indicates that said subject has a *Chlamydia* infection.

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